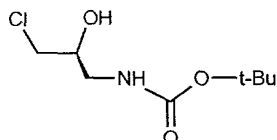


120.83, 124.67, 127.65, 138.06 and 155.40 ; MS (EI), m/z (relative intensity) 222 (37) and 164 (100).

EXAMPLE 3

5



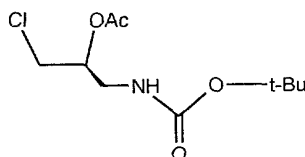
10 **Preparation of tert-butyl (2S)-3-chloro-2-hydroxypropylcarbamate, alternatively named N-((2S)-3-chloro-2-hydroxypropyl)(tert-butoxy)carboxamide (Compound IV, R³=t-butyl, X=Cl)**

To a slurry of (2S) 1-amino-3-chloro-2-propanol hydrochloride, (750.3 g, 5138 mmol) in methylene chloride (2728 g) and methanol (435.4 g) at -13°C was
15 added a solution of di-tert-butyl dicarbonate (1178.3 g, 5399 mmol, 1.05 eq) in methylene chloride (1144 g) followed by triethylamine (572.3 g, 5656 mmol, 1.10 eq). The resultant 13°C slurry was then warmed and stirred at 17-19°C for 1 h. The resultant solution was concentrated under reduced pressure to a 2182 g slurry. Toluene (959.3 g) and water (975.5 g) were added and the phases separated. The
20 organic phase was washed with water (500 ml) and the aqueous serial back extracted with toluene (2 X 500 ml). The combined organics were concentrated under reduced pressure to 1592 g. Isooctane (5853 g) was added and the mixture seeded and stirred at 20-25°C for 17 h. The precipitated product was collected by vacuum filtration, washed with isooctane (400 g) and dried in a nitrogen stream to afford Compound IV,
25 wherein R³=t-butyl, X=Cl, (1024 g, 95.1 %): GC retention time = 8.2 min (15 meter DB5 capillary column, 70°C for 2 min, then ramp 10°C/min); ¹H-NMR (CDCl₃, 400 MHz) δ: 5.08 (bs, 1H), 3.92 (m, 2H), 3.57 (bs, 1H), 3.55 (m, 1H), 3.42 (m, 1H), 3.24

(m, 1H), 1.45 (s, 9H); ^{13}C -NMR (CDCl_3 , 100 MHz) δ 28.35 (q), 43.90 (t), 46.52 (t), 71.23 (d), 80.13 (s), 157.24 (s).

EXAMPLE 4

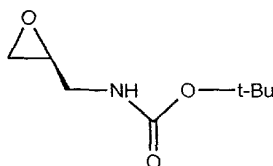
5



10 **Preparation of (1S)-2-[(tert-butoxycarbonyl)amino]-1-(chloromethyl)ethyl acetate, alternatively named N-((2S)-3-chloro-2-acetoxypropyl)(tert-butoxy)carboxamide (Compound V, $\text{R}^3 = \text{t-butyl}$, $\text{R}^4 = \text{Ac}$, $\text{X} = \text{Cl}$)**

To a solution of tert-butyl (2S)-3-chloro-2-hydroxypropylcarbamate
15 (0.9928 g, 4.74 mmol) in THF (7 ml) and triethylamine (0.7303 g, 7.22 mmol, 1.52 eq) was added acetic anhydride (0.6033 g, 5.91 mmol, 1.25 eq) and N, N-dimethyl-4-aminopyridine (0.00265 g, 0.0217 mmol, 0.0046 eq). The solution was stirred at room temperature for 3 days. Toluene (10 g) and saturated aqueous sodium bicarbonate (10 ml) was added and the phases separated. The aqueous was washed
20 with a mixture of toluene (10 ml) and THF (5 ml) and the combined organics dried on magnesium sulfate. The organics were concentrated under reduced pressure to 1.6 g and heptane (7.3 g) added. After standing for 25 days at 20-25°C, a precipitate formed. Heptane (10.8 g) was added and the precipitate collected by vacuum filtration, washed with heptane (10 ml) and dried in a nitrogen stream to give
25 Compound V, wherein $\text{R}^3 = \text{t-butyl}$, $\text{R}^4 = \text{Ac}$, $\text{X} = \text{Cl}$, 0.3803 g (31.9%): ^1H -NMR (400 MHz, CDCl_3) δ : 1.45 (s, 9 H), 2.11 (s, 3 H), 3.41 (m, 2 H), 3.67 (m, 2 H), 4.79 (s, 1 H), 5.07 (t, $J = 5.2$ Hz, 1 H); ^{13}C NMR (CDCl_3) 20.92 (q), 28.33 (q), 41.43 (t), 43.30 (t), 72.16 (d), 79.89 (s), 155.85 (s), 170.26 (s); MS (EI) for $\text{C}_{10}\text{H}_{18}\text{ClNO}_4$ m/z 251 M^+ ; $[\alpha]_D^{22}$ (-2, $C = 1.0$, methylene chloride); Anal. Calcd for $\text{C}_{10}\text{H}_{18}\text{ClNO}_4$: C, 47.72; H, 7.21; N, 5.57. Found: C, 47.70; H, 7.17; N, 5.55.
30

EXAMPLE 5



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**Preparation of tert-butyl (2S)oxiranylmethylcarbamate, alternatively named N-
[[(2S)oxiran-2-yl)methyl](tert-butoxy)carboxamide (Compound II, R³ =t-butyl,
X=Cl)**

10

To a solution of tert-butyl (2S)-3-chloro-2-hydroxypropylcarbamate (19.98 g, 95.29 mmol) in methanol (50.0 ml) at 13 °C was added lithium t-butoxide (8.40 g, 104.9 mmol, 1.10 eq) while maintaining less than 22 °C. The mixture was stirred at 8 to 20 °C for 15 min and water (200 ml) followed by methylene chloride (200 ml) was added. The phases were separated and the aqueous washed with

15

methylene chloride (135 ml). The combined organics were dried on magnesium sulfate and concentrated to an oil. Column chromatography on silica gel (0 to 4% methanol in methylene chloride eluent) gave Compound II, wherein R³ =t-butyl, X=Cl, as a white solid (14.26 g, 86.4%): m.p. 45-49 °C; ¹H NMR (400 MHz, CDCl₃) δ: 1.448 (s, 9 H), 2.59 (s, 1 H), 2.78 (t, J = 4 Hz, 1 H), 3.09 (s, 1 H), 3.20 (dt, J = 14, 6 Hz, 1 H), 3.53 (d, J = 15 Hz, 1 H), 4.85 (s, 1 H); ¹³C NMR (CDCl₃) 28.28 (q), 41.72 (t), 45.04 (t), 50.85 (d), 79.61 (s), 155.96 (s); MS (CI⁺) for C₈H₁₅NO₃ m/z 174 (M+H)⁺; [α]_D²² (-13, C + 1.0, methylene chloride); Anal. Calcd for C₈H₁₅NO₃: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.17; H, 8.54; N, 8.00.

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